August 26, 2002

John E. Heinze, Ph.D.
Senior Vice President
John Adams Associates Inc.
The Council for LAB/LAS Environmental Research
529 14th Street, N.W. Suite 655
Washington, D.C. 20045

Dear Dr. Heinze:

The Office of Pollution and Toxics is transmitting EPA's comments on the robust summaries and test plan for Benzene, C6-12 Alkyl Derivatives posted on the ChemRTK HPV Challenge Program Web site on December 17, 2001. I commend The Council for LAB/LAS Environmental Research for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The Council for LAB/LAS Environmental Research advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Benzene C6-C12 Alkyl Derivatives

SUMMARY OF EPA COMMENTS

The sponsor, Huntsman Corporation, submitted a test plan and robust summaries to EPA for benzene, C6-C12 alkyl derivatives (CAS No. 68608-80-0) dated November, 2001. EPA posted the submission on the ChemRTK HPV Challenge Website on December 17, 2002.

EPA has reviewed this submission and reached the following conclusions:

1. Chemical Definition. The submitter needs to provide additional information for the following: (a) the relationship of the test substance to the title substance; (b) the compositions of "Alkylate Top@ and analogs used in the supporting studies; and (c) how the test results support the submitter=s decision to conduct no additional testing.

2. Physicochemical Properties and Environmental Fate. The submitter needs to provide measured biodegradation data for benzene, C6-12 alkyl derivatives. The submitter needs to provide data for transport and distribution because it is an HPV Challenge Program endpoint.

3. Health Effects. The submitter needs to provide sufficient rationale for the extrapolation of the submitted data to the title substance. In addition, many of the robust summaries were not adequate to permit the evaluation of the submitted data. The test plan and supporting robust summaries need further development to support the conclusion that additional testing is not needed.

4. Ecotoxicity. The reported log K_{ow} values suggest that the submitter needs to conduct chronic toxicity testing in invertebrates on benzene, C6-12 alkyl derivatives.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE BENZENE C6-12 ALKYL DERIVATIVES CHALLENGE SUBMISSION

Test Plan

Use of Analog Data. Three elements of the test plan and robust summaries need additional explanation or information: (a) the relationship of the test substance to the title substance; (b) the composition of the test substance and analogs used in the supporting studies; and (c) a discussion of how the test results presented in the test plan and robust summaries support the submitter's decision to conduct no additional testing.

The submitter notes that "Benzene, C6-C12 alkyl derivatives" is the same as "Alkylate Top," a process stream that typically contains 55% C9 and C10 alkylated benzenes and 38% C14 and C15 *n*-paraffins. This substance is produced during the manufacture of linear alkyl benzenes (LABs) and is isolated as an "intermediate distillation cut prior to the isolation of [a] final LAB product." It would be useful for the submitter to discuss whether the Alkylate Top as defined in the test plan characterizes the majority of manufactured products that might be classified as benzene, C6-C12 alkyl derivatives.

The submitter presents data for Alkylate Top and analogs or components of the test substance. The composition of both Alkylate Top and these analogs are not always clearly described. Examples include the following:

- In the AEnvironmental Fate@ section of the test plan and in the robust summaries, Alkylate Top and L210L from 1980 are described as containing A29% paraffin, 44% alkylbenzene and 24% indanes,@ and it is noted that the modern Alkylate Top contains Avirtually no indanes.@ Both Alkylate Top and L210L, however, are used in other studies from the 1970s and 1980s without mention of the composition (for example, L210L is used in robust summaries on pages 21/44, 28/44, and 31/44).

- L210H is used in another study. This substance is described as Aessentially the same material@ as L210L, but the submitter did not provide composition data for either material.

- AAlkylate 215@ is associated with CAS No. 67774-74-7 (ABenzene, C10-C13 alkyl derivatives@) on robust summary page 12/44 and with benzene, C10-C16 alkyl derivatives on page 38/44, but the composition is not presented.

- APhenyl-C10 (C10 LAB)@ is associated with CAS No. 67774-74-7 on robust summary pages 10/44 and 21/44 and no CAS number on page 24/44.

- Many studies used benzene, C10-C13 alkyl derivatives but there was no discussion about whether paraffins were contained in this test substance.

The submitter needs to describe completely the composition of all analogs so that their relationship to Alkylate Top can be fully understood.

The submitter intends to review and evaluate Athe available environmental fate and toxicity data for the principal constituents of the mixture@ in order to help characterize Alkylate Top. This includes the use of test data obtained from older Alkylate Top streams and mixtures of secondary alkylbenzenes (i.e., C10 and C10-C13 alkyl benzenes), two primary alkyl benzenes (i.e., decylbenzene and nonylbenzene), and two linear alkanes (i.e., n-tetradecane and n-pentadecane). The use of the older Alkylate Top needs specific discussion, since its composition differs from the currently-produced product. For example, while the submitter describes the implication of using the older Alkylate Top containing indanes in the Environmental Fate section, no such explanation is presented in the Health Effects section. In addition, it is not apparent whether *n*-paraffins are included in all compositions of Alkylate Top. The submitter needs to describe clearly how the data from the chemical analogs and older Alkylate Top will be used to characterize the modern Alkylate Top.

<u>Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility)</u>

The submitted data are adequate for the purposes of the HPV Challenge Program.

<u>Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)</u>

The submitted photodegradation data and the rationale provided for stability in water are adequate for the purposes of the HPV Challenge Program.

Transport and Distribution in the Environment. The submitter incorrectly states that this is not an HPV Challenge Program endpoint. The HPV Challenge Program clearly indicates that this endpoint needs to be addressed (see http://www.epa.gov/chemrtk/sidsappb.htm for guidance).

When developing the fugacity model, the submitter needs to provide the assumption and data inputs to the model (see Guidance for Robust Summary preparation).

Biodegradation. The submitter provided information on a 35-day biodegradation test for benzene, C6-12 alkyl derivatives. EPA finds the data inadequate because the submitter did not follow OECD Guideline 301. Under this Guideline, a biodegradation test lasts for 28 days, but may be prolonged beyond 28 days when biodegradation has started but no plateau has been reached by day 28. The submitter did not

indicate whether this was the case. The submitter needs to provide measured biodegradation data on benzene, C6-12 alkyl derivatives following OECD Guideline 301 and report the composition of the sample tested.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

There are no data provided on the toxicity of the currently produced Alkylate Top. The data available are for an older Alkylate Top of different composition, or for components or analogs of Alkylate Top. As indicated above, the relationship of data for these substances to the potential effects of Alkylate Top needs to be fully discussed to permit an evaluation of the data and their use to assess the mammalian toxicity of Alkylate Top.

The full evaluation of the mammalian toxicity data in the robust summaries was limited by the general lack of detailed descriptions of the methods used and results obtained, and the use of secondary sources of data for the preparation of the robust summaries.

Acute Toxicity. Information in the robust summaries for the acute oral and inhalation toxicity of the older Alkylate Top appears to address this endpoint for the purposes of the HPV Challenge Program; however, it is not clear how the tested substance relates to the currently-produced Alkylate Top.

Repeated-Dose Toxicity. EPA reserves judgement on the adequacy of the repeated-dose data pending clarification of use of the C10-C13 LAB to represent the Alkylate Top and the addition of more details to the robust summaries for both LAB and tetradecane.

Genetic Toxicity. EPA reserves judgement on the adequacy of the robust summaries of studies using C10-C13 LAB pending information on whether the test substance included any *n*-paraffins. The submitter needs to conduct additional testing for both genetic mutations and chromosomal aberrations if the test material did not include the paraffins that are present in Alkylate Top.

Reproductive Toxicity. EPA cannot fully evaluate the submitter=s plan to conduct no further testing. Although an adequate robust summary of the reproductive toxicity of LAB was provided, no discussion of its applicability to Alkylate Top was provided and no summaries for the *n*-paraffin portion of Alkylate Top were provided.

Developmental Toxicity. EPA cannot fully evaluate the submitter=s plan to conduct no further testing. Although an adequate robust summary of the developmental toxicity of alkylate 215 was provided, this material was identified in the robust summary as an analog of LAB, which itself is an analog of Alkylate Top. No discussion was provided to support the use of Aalkylate 215@ as an analog of Alkylate Top, and no robust summaries or discussion were provided for the *n*-paraffin portion of Alkylate Top.

Ecological Effects (fish, invertebrates, algae)

Invertebrates. EPA recommends that a 21-day chronic reproductive study in daphnia (OECD Guideline 211) be conducted in accordance with guidance on chemicals that have log Kow values between 4.2-7.25 (65 FR 81686). This test should be conducted using benzene, C6-12 alkyl derivatives and should report the composition of the sample tested. Because of the low water solubility of these chemicals, the submitter should consult the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures available at http://www.oecd/org/ehs/test/monos.htm.

Specific Comments on the Robust Summaries

Health Effects

Acute toxicity. The robust summaries for the acute oral, inhalation, and dermal toxicity of LAB and the dermal toxicity of Alkylate Top lacked a number of details on the experimental methods and results. In particular, the clinical signs observed at each concentration should be described. Other missing details included the strain of animals tested, dose levels, and number of animals per dose level.

Repeated-Dose Toxicity. The robust summaries of repeated-dose toxicity studies for LAB were prepared from a secondary source and lacked complete descriptions of methods and results. The submitter needs to add detailed information on methods and results to the summary of tetradecane, which was also prepared from a secondary source and reported only the LOAEL (also described as a TDLo).

Genetic Toxicity. The robust summaries lacked details including the results of positive control substances used, the types of detailed results observed, the statistical significance of observed effects, and the concentration at which cytotoxic effects (if any) were observed.

Ecological Effects

The robust summaries were missing required data elements (including test substance purity, number of organisms per concentration, control use and response, and water chemistry parameters). In addition, the summaries often did not identify the substance and concentration of the solubilizing agent when this type of chemical was used.

Fish. The first acute fish robust summary indicates that the test substance Awas comprised of 93% alkylbenzenes and 18% phenylalkanes.@ Since the sum of the percentages is more than 100% and alkylbenzenes and phenylalkanes refer to the same basic structure, the meaning (and accuracy) of this is unclear. The submitter needs to explain this statement.

Invertebrates and Algae. One acute daphnia and one algal toxicity summary provided data from more than one study. The submitter needs to submit individual robust summaries for each test conducted.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.